4

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/814,646	04/01/2004	Daniel G. Wright		7540

7590 07/15/2005

MARY HELEN SEARS
THE M.H. SEARS LAW FIRM, CHTD.
Suite 800
910 Seventeenth Street, N.W.
Washington, DC 20006

EXAMINER	
BARNHART, LORA ELIZABETH	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 07/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/814,646	WRIGHT ET AL.	
	Examiner	Art Unit	
	Lora E. Barnhart	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

5.0.0

DETAILED ACTION

Specification

The use of the trademark "CHEMSTRIP 2LN" has been noted in this application. This and all other trademarks should be capitalized wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks.

Additionally, the specification refers to a "Hofmann-LaRoche[*sic*] Chemstrip 2LN". The examiner requests clarification, since the CHEMSTRIP 2LN product appears, according to a MEDLINE search, to be a product of Boehringer Mannheim Diagnostics Inc. Applicant should specify whether the specification contains an inadvertent error or whether it refers to some distinct, but undescribed, product of Hoffmann-La Roche Inc.

Claim Objections

Claim 1 is objected to because of the following informalities: It recites "chemilumines imparting", which should read "chemiluminescence-imparting" (step (b), part (ii)). In addition, the commas at the ends of steps (a)-(d) (*i.e.* after the words "minute", "product", "develops", and "chemiluminescence", respectively) should be replaced with semicolons for clarity. In addition, "fluorescence imparting" at step (b), part (ii), should read, "fluorescence-imparting".

Claim 2 should be amended to recite "mouthwash" (one word) at line 1.

Claim 4 should be amended to recite "time interval" at line 2.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

M.P.E.P. § 2163 recites, "An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention... one must define a compound by 'whatever characteristics sufficiently distinguish it'. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to **immediately envisage** the product claimed from the disclosed process."

Claim 1, step (b), part (i) requires "a chemical compound that is cleaved into at least two fragments when exposed to the action of an enzyme known to be characteristically present in human neutrophils". Claim 1, step (b), part (ii) requires "a dye precursor...in sufficient quantity to react completely with one of said fragments to form a colored...product". The specification does not describe any way in which an enzyme might be determined to be "characteristically present" on or in neutrophils; the

disclosure is limited to human neutrophil elastase. The specification also does not describe any way in which a cleavable compound might be elucidated for a given enzyme; the disclosure is limited to an indoxylcarboxylic ester. Finally, the specification does not describe any way in which a dye might be chosen that reacts with one of the fragments resulting from the cleavage of any compound by any neutrophil-specific enzyme; the disclosure is limited to some unknown diazonium salt that forms a purple product on reaction with the cleavage product of indoxylcarboxylic ester.

Although the specification points out one combination effective in indicating the presence of active neutrophil-specific enzyme (*i.e.* indicating the presence of active neutrophil elastase by reacting it with some indoxylcarboxylic ester and detecting a violet dye resulting from the interaction of some cleavage product and some diazonium salt), the components required for the claimed method are not particularly and specifically described within the specification. No structure is provided for the indoxylcarboxylic ester or for the diazonium dye. In short, the skilled artisan could not immediately envisage the products recited in the claims.

The claims are currently in means-plus-function form; M.P.E.P. §2163 teaches that such claims are adequately described if "the written description adequately links or associates adequately described particular structure, material, or acts to the function recited in a means-plus-function claim limitation", or if "it is clear based on the facts of the application that one skilled in the art would have known what structure, material, or acts perform the function recited in a means-plus-function limitation". The instant disclosure does not meet either of these criteria. As detailed above, the specification

does not link any specific compound to the claimed activity, and because of the diversity of the genus of reactive compounds and indicative dyes, even if these genuses are limited to comprise only esters and diazonium dyes, the skilled artisan would not be able to determine which modulators do or do not perform the claimed function without extensive experimentation. See 35 U.S.C. §112, sixth paragraph.

Because claims 2-4 depend from inadequately described claim 1 and do not issue of adequate written description, they must also be rejected under 35 U.S.C. 112, second paragraph.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites a method that allegedly is performed "with an exceptional degree of sensitivity, accuracy, and precision", which is confusing. The term "exceptional" is a relative term and is meaningless without a point of reference. The claim does not provide another method to which the instant method could be compared. Clarification is required.

Claim 1, step (a), recites the limitation "said person" in line 1. There is insufficient antecedent basis for this limitation in the claim. The preamble does not recite a person. Clarification is required.

Claim 1, step (b), part (i), recites the limitation "the target enzyme" in line 4. There is insufficient antecedent basis for this limitation in the claim. The claim does not recite a target enzyme. Clarification is required.

Claim 1, step (c), recites "allowing said sample...to remain in contact", which is confusing. It is not clear whether said "allowing" comprises an active process step. Clarification is required. The examiner suggests the use of the term "incubating".

Claim 1 is further indefinite because it omits essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: At step (e), the relationship between a given intensity of color, fluorescence, or chemiluminescence and the number of neutrophils in the sample is not particularly pointed out within the claim. Clarification is required.

Because claims 2-4 depend from indefinite claim 1 and do not clarify the point of confusion, they must also be rejected under 35 U.S.C. 112, second paragraph.

Claim 2 is further indefinite in that it recites "a saline/bicarbonate buffer", which is confusing. It is not clear whether the buffer necessarily comprises both saline and bicarbonate, or only one of these. Clarification is required.

Claim 2 is further confusing in that it recites "a distinct color". It is not clear how the color of claim 2 might be distinguished from any other color, or on what scale distinctiveness is measured. Clarification is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wright et al. (1986, *Blood* 67: 1023-1030; reference U) taken in view of Scheer (1987, *Am. J. Clin. Pathol.* 87: 86-93; reference V) and Taylor et al. (1975, *Arch. Biochem. Biophys.* 169: 91-101; reference W). The claims are drawn to a method for determining an individual's mucosal neutrophil count comprising obtaining an oral mucosal sample and delivering a quantity of said sample to a test strip, said strip comprising a compound that is cleaved by an enzyme present in neutrophils and a dye that reacts with the cleavage products, forming a detectable product. In some dependent claims, the buffer, compound, and dye are specified. In some dependent claims, the sample is collected after 30 seconds of washing.

Wright et al. teach that an accurate neutrophil count may be obtained from mouthwash samples (Figures 2-4). The sample collection procedure of Wright et al. comprises allowing an individual to wash his/her mouth for 30 seconds with sterile saline (page 1024, column 1). Wright et al. does not teach the use of a compound that

can be cleaved by an enzyme present in neutrophils and a dye that reacts with the cleavage products, forming a detectable product.

Scheer compares two test strips that detect the presence of leukocyte esterase (page 86, column 2, through page 87, column 1). Said strips comprise an indoxylcarbonic acid ester that is a substrate of leukocyte esterase and a diazonium dye that produces a purple color (page 86, columns 1 and 2).

Taylor et al. teach that leukocyte elastase has esterase activity (page 92, column 1, and page 94, column 1).

A person of ordinary skill in the art would have had a reasonable expectation of success in substituting the test strips of Scheer into the method of Wright et al. because Wright et al. teach that the oral mucosa mouthwash sample comprises neutrophils, and because Scheer teaches that the test strips detect leukocytes, including neutrophils. The skilled artisan would have been motivated to make said substitution because the method of Scheer allows fast, quantitative detection of neutrophils, while the detection method of Wright et al. requires expensive microscopy equipment and skilled practitioners.

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was made to substitute the test strips of Scheer into the method of Wright et al. because Wright et al. teaches that the disclosed sample comprises cells that react with the test strips of Scheer.

Therefore, the invention as a whole would have been *prima facie* obvious to a person of ordinary skill at the time the invention was made.

No claims are allowed. No claims are free of the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lora E. Barnhart whose telephone number is 571-272-1928. The examiner can normally be reached on Monday-Friday, 8:00am - 4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lora E Barnhart

LEB

SANDRA E. SAUCIER
PRIMARY EXAMINER